

exempt from the necessity of bodily labour, I may quote my own experience. Although seven or eight cases have been referred to me in private practice, as supposed cases of Addison's disease, only two of these have been true cases of the disease, and I have met with no others amongst persons of the middle and higher classes. I believe, too, that in this respect, the experience of all other physicians will be found to coincide with mine.

From these data, therefore, imperfect as they are, the following deductions may safely be drawn.

The occurrence of Addison's disease takes place almost exclusively in persons employed in active manual labour.

The mortality caused by it is pretty equally distributed over the laborious period of life, and to that period it is almost entirely confined.

The disease is comparatively much more frequent in persons of the male sex, whose employment naturally involves the heaviest kinds of labour.

Lastly, a preponderating number of the cases which occur in persons of the male sex are found amongst those classes of labourers whose occupations are most likely to expose them to bodily injury from accident or over-exertion.

The facts thus brought out cannot fail to suggest obvious inferences as to the probability that, in many of these cases, more or less temporary causes of local inflammation may have existed, similar to those which appear to have been the starting point of the disease in some of the cases to which I have specially referred. In persons of the working classes, strains and falls, which do not involve disabling consequences, are soon forgotten, and therefore seldom reported; whilst the necessity of striving against the weakness induced by a strain or blow may tend to keep up an inflammatory process, which would have naturally subsided under favourable conditions of rest. Without, therefore, venturing to speak dogmatically on a point which can only be cleared up by much future investigation, I may yet say that I incline to believe the origin of Addison's disease, in many of the unexplained cases, to be due to traumatic causes, although its development has probably been favoured by certain constitutional proclivities.

Very few words need be said here with respect to the diagnosis and prognosis of Addison's disease. The diagnosis is founded upon the constitutional symptoms, aided, in a large majority of cases, by the presence of more or less of the peculiar change of colour in the skin. It is not always unattended with difficulty, but, to those who have any practical acquaintance with the disease, it is not, I think, more doubtful than the diagnosis of many other chronic diseases. The prognosis is, of course, invariably grave as regards the ultimate result, though it is impossible to say to what extent life may be prolonged under favourable circumstances. Rest and scrupulous avoidance of bodily or mental excitement, or any other causes of nervous exhaustion, form the essential parts of the therapeutical management of all such cases; whilst the diet and medical treatment must be carefully adapted to the inevitably varying phases of the disease.

It only remains for me to sum up, in conclusion, the objects which I have had in view in the course of lectures which I have had the honour to deliver before you.

In the first, I believe I delineated faithfully all the principal clinical symptoms of Addison's disease, and the remarkable varieties in their course; together with the true characters of the pathological lesions in and around the suprarenal capsules, which have been found to coexist with them.

In the second lecture, I endeavoured to show clearly, on the one hand, the concurrent testimony of facts in proof of the real connection subsisting between these clinical symptoms and the one specific lesion in the suprarenal capsules, and, on the other, the baseless nature of the misconceptions which have prevented the general recognition of its reality.

In to-day's lecture, I have trodden on more difficult ground. No one can feel more strongly than myself that the opinions which I have been led to form, with respect to the obscure pathological and etiological processes in Addison's disease, rest as yet upon an inadequate basis. I can only express the hope that, however problematical their correctness may appear to many, the suggestions I have ventured to make, regarding the probable mode of production of the symptoms of Addison's disease, and the probable means of origin of the suprarenal disease itself, may lead to a thorough investigation, in future cases, of all the facts bearing upon these questions; and thus, to the acquisition of knowledge which may justify positive conclusions, in place of the uncertain inferences which are all that I have been able to draw, from my own necessarily limited personal experience, and the insufficient materials at my command.

THE GERM-THEORY OF DISEASE:

BEING A DISCUSSION OF THE RELATION OF BACTERIA AND ALLIED ORGANISMS TO VIRULENT INFLAMMATIONS AND SPECIFIC CONTAGIOUS FEVERS.

By H. CHARLTON BASTIAN, M.D., F.R.S.,

Professor of Pathological Anatomy in University College, and Physician to University College Hospital.*

WHEN honoured by a request from the Council of this Society, a few weeks since, to open a debate during the current session, compliance with such a wish was regarded by me as a professional duty. I was compelled, therefore, to do the best I could with the short time and limited leisure which presented themselves, though these, I regret to say, have proved insufficient to enable me to bestow the attention I should have desired upon the vast accumulation of writings directly or indirectly related to the subject selected for discussion, and quite insufficient also to enable me to throw light upon it, to the extent I should have wished, by certain new observations of my own. The subject, however, large as it is—and consequently difficult to be dealt with satisfactorily in the space of one hour—seemed to recommend itself for several reasons. (1) It is a question lying at the root of the pathology of the most important and most fatal class of diseases to which the human race is liable—diseases which cause nearly one-fourth of the total number of deaths in this country. (2) It is a subject important alike to those engaged in almost every department of our profession. And (3) it is one which I happen to have very carefully considered for several years, and for the elucidation of which I was tempted in 1869 to undertake long and laborious investigations, though these may have seemed to many to have little practical bearing upon the science of medicine.

The subject of the relation of the lower organisms to disease has, moreover, a growing importance. The notion that there is a distinct causal relation between the two—though it has long existed in one form or another—is one which has been spread enormously within the last few years, partly owing to our increase of knowledge concerning these low organisms, and partly because of their ascertained presence in numerous diseased tissues and exudations. Medical literature, both at home and abroad, now in fact teems with papers and memoirs bearing upon this relation, and such communications rapidly increase in number year by year.

In the short time allotted to me to open the debate, I shall be able to make specific allusions to but few of these contributions, as it would seem better to keep the broad issues well in view in my opening statement, and to reserve questions of detail, as these may be taken up by other speakers and subsequently commented upon where necessary.

The one common and distinguishing feature peculiar to all the diseases, whose pathology we are now about to consider, is their "contagiousness". An individual affected by either of them throws off particles from the region specially affected, or from many parts of the body; and these particles, on coming into contact with suitable surfaces in other persons, may incite similar local or general diseases—though such results do not invariably follow. This peculiarity, by means of which such diseases are spread amongst the members of a community, was, even in the time of Hippocrates, compared to the property by which one fermenting mass may communicate its state of change to another mass of fermentable material. Throughout all intervening periods such an analogy has never been lost sight of—it has rather been more and more strongly dwelt upon. Thus, more than two centuries ago, we find, as has been recently pointed out, Robert Boyle, one of our great English philosophers, and himself a pioneer in scientific investigation, giving strong expression to the then current view. "He that thoroughly understands", he says, "the nature of ferments and fermentations, shall probably be much better able than he that ignores them, to give a fair account of several diseases (as well fevers as others) which will perhaps he never thoroughly understood without an insight into the doctrine of fermentation." Again, in more recent times, it was doubtless under the influence of a belief in the same analogy between fermentations and the class of diseases of which I am about to speak, that the term "zymotic" was proposed by Dr. Wm. Farr, and adopted as a general designation, under which nearly all these diseases might be included. The consequence of the adoption of this nomenclature has been, that views as to the nature of the infecting something or *contagium* have since been so powerfully influenced as to

* Read before the Pathological Society of London, April 6th.

be actually led by views at the time entertained concerning the nature of *ferments*. The relationship supposed to exist between zymosis and fermentation has indeed been stamped and ratified by the very general consent of the profession.

Omitting for the present any remarks as to the real strength of this analogy, I would merely further point out that the foundations of the "germ-theory of disease", in its most commonly accepted form, were laid in 1836 and shortly afterwards. The discovery at this time of the yeast-plant by Schwann and Cagnard-Latour soon led to the more general recognition of the almost constant association of certain low organisms with the different kinds of fermentations. But it was not till twenty years afterwards that Pasteur announced, as the result of his apparently conclusive researches, that low organisms acted as the invariable causes of fermentations and putrefactions—that these, in fact, though chemical processes, were only capable of being initiated by the agency of living units. If, in accordance with this somewhat narrow and exclusive view, living units were to be regarded as the sole producers of fermentation and putrefaction, then they were the sole ferments. The extension of this doctrine by medical men to contagious diseases, in face of the analogy sanctioned by the use of the term "zymotic", became only too easy. It was obviously nothing but the logical outcome of the two sets of views, to hold that low organisms were the true contagia or sole "germs" of the so-called zymotic diseases.

It so happens, therefore, that the very exclusive notion just mentioned, as to the nature of contagia, is at present almost as deeply rooted in the minds of the majority of writers on epidemic diseases and contagious fevers as was the opposite notion, founded upon the physico-chemical doctrine of Liebig some twenty years ago. Then a ferment was regarded as a portion of organic matter (not necessarily living) in a state of molecular change ("motor decay"), which, by virtue of its own unstable nature, was capable of communicating molecular movement (chemical change) to other unstable or fermentable mixtures. This broader notion was promulgated by Liebig, at a time when less was known than at present as to the constant association of low organisms with the processes of fermentation and putrefaction. The nature of this relationship was, in fact, never adequately grappled with by him. Still, views of this kind, promulgated by Liebig, would not give anything like the same support to the germ-theory of disease as that afforded by the doctrines of Pasteur. Those who have adopted and developed Liebig's views now hold that living organisms, though they may operate as ferments, act in this capacity merely by virtue of the chemical changes which the carrying on of their growth necessitates; and that other chemical changes, taking place during the decay of organic matter, may make fragments of it (in the dead state) almost equally capable of initiating fermentative changes in suitable media, whilst in either case Bacteria or allied organisms are prone to be engendered as correlative products.

In the present day, therefore, two questions seem to need the serious consideration of medical men. In the first place, it may be asked, Are we justified in relying so strongly upon the analogy between fermentation and zymosis? Secondly, we may inquire whether the researches by which Pasteur claims to have established the sole nature of ferments are so conclusive as they have been commonly regarded. In reply to the first question, certain qualifying considerations will hereafter be stated, though it may be at once admitted that the analogy is so strong as to make it likely to continue to exercise a very considerable influence upon medical opinion. It therefore becomes all the more necessary for medical men to look to the foundations of Pasteur's doctrine, if they are not prepared blindly to follow his dicta on a subject which is of so much importance for medical science. It was with this view that I undertook a few years ago, and shortly after I had been called upon to teach pathology, a series of investigations bearing upon this subject. In consequence of this work, I was compelled, as others had been, to refuse assent to the exclusive doctrines of Pasteur concerning the nature of ferments. I do not enter upon this discussion now. I maintain, however, that my own investigations and those of others show that units of living matter are not the sole ferments, since fermentation and putrefaction may be initiated in their absence, and since it can be shown that mere particles or fragments of organic matter may act in this capacity. For a brief exposition of the grounds of this belief, I would refer those interested in the matter to my recently published work, *Evolution and the Origin of Life*.

Some time must be allowed to elapse before anything approaching to general agreement can be expected on such a subject; and, meanwhile, standing as we do in the face of opposite doctrines as the nature of ferments, we are free to look into the question of the relation of the lower organisms to disease on its own merits—apart, that is, from the overweighing influence of any general theory of fermentation.

Leaving on one side, therefore, the influence of the analogy deemed

to exist between the process of fermentation and that of zymosis, we may ask what other general evidence is forthcoming in favour of the notion that contagia are low organisms or living units, rather than dead organic particles from altered tissue-elements, or complex chemical compounds of alkaloidal constitution engendered in the tissues or in some of the fluids of the body. The consideration of this question may be introduced by a quotation from Dr. Burdon Sanderson's valuable report on the "Intimate Pathology of Contagion" (Twelfth Report of the Medical Officer of the Privy Council, 1870, p. 243). He says: "There are two obvious objections which stand in the way of the acceptance of any chemical explanation of the phenomena of contagion. The first is, that the multiplication of contagium in the body of the infected individual is a process which cannot be compared to any which is brought about by chemical agencies independently of organic development. The second is, that all contagia possess the power of retaining their latent virulence for long periods (often resisting the most unfavourable chemical and physical conditions), and only show themselves to be what they are when they are brought into contact with [the] living organism. Outside of the body, the contagious material withstands all those changes to which, on chemical grounds, we should expect it to be liable; while in the body it manifests a degree of activity, and gives rise to an amount of molecular disturbance, which is quite as unaccountable.....Neither of these difficulties stands in our way if we suppose that the contagious process is connected with the *unfolding of organic forms*."

Now, although this is about as strong a statement as can be made, from an *à priori* point of view, against the mere chemical action of contagium and in favour of a germ-theory, I must confess that neither of the considerations seems to me to carry very much weight with it. I should be inclined to say, in reply (1), that proof is altogether wanting of the "multiplication of contagium" in the body in the same sense that a living unit multiplies; and that there are physico-chemical processes which may illustrate what occurs when contagium increases within the system. Instead of an increase by continuous organic development and multiplication, it may be that contagium augments by some such process as that by which crystals of sulphate of soda increase or "multiply" when a fragment of such a body is thrown into a complex fluid containing its component elements. This is confessedly a very imperfect illustration, and one to which I resort merely to indicate the possible occurrence of another mode of increase of contagium within the body; though, in an infected animal, such increase may occur in a much more subtle manner, owing to the fact that fluids altered, directly or indirectly, by the original contact of contagium with some part of the body, are either locally or generally brought into intimate relation with the active, though modifiable, living units of the various tissues. And (2), in reply to Dr. Sanderson's other objection, which stands, as he supposes, in the way of any chemical explanation of the phenomena of contagion, I should say that, although our knowledge is at present extremely vague concerning the power possessed by the various contagia of retaining their virulence for long periods, and of resisting unfavourable physical and chemical conditions, we have no reason to believe that the more complex combinations of which living matter is composed are capable of resisting influences which would prove destructive to less highly complex not-living substances—such as snake-poison, woorara, or other compounds of this class. The general evidence is, therefore, as I read it, certainly not more favourable to a vital or germ theory than to a physico-chemical theory, as regards the nature and action of contagia.

I should here point out, however, that under the term "germ-theory" two distinct views are included, each having its advocates amongst distinguished members of this Society. The side to which Dr. Sanderson leans is sufficiently obvious. Speaking of contagious particles, he says (*loc. cit.*, p. 255): "With reference to their mode of action, we have examined into those considerations which seem to render it probable that they are *organised beings, and that their powers of producing disease are due to their organic development*; and we have accepted this doctrine as the only one which affords a satisfactory explanation of the facts of infection."*

This is the doctrine with which we are at present especially concerned, though it may be well for me to say a few words concerning the other sense in which a "germ-theory of disease" is maintained by a distinguished member of this Society. Dr. Beale says (*Disease-Germs, their Real Nature*, 1870, p. 5): "We have, therefore, now to inquire what is the material substance which passes from the diseased to the

* These words occur in a summary which, it is only right to add, was immediately prefaced by the following statement. "The sentences which follow must therefore be accepted by the reader as nothing more than indications of the questions we are trying to solve, or as forecasts of what we hope to establish or disprove by experiment."

healthy organism in small-pox, in measles, in scarlet fever, and other allied contagious diseases from which man and domestic animals suffer so severely. *The material in question grows and multiplies and produces its kind, as all living things do, and as nothing that does not live has been proved to be capable of doing.* We may, therefore, conclude that it is living matter." And, as to the derivation of such matter, Dr. Beale says, "a disease-germ is probably a particle of living matter derived by direct descent from the living matter of man's organism", though he supposes it to be altered and degraded as regards formative power by previous rapid multiplication of the tissue-elements or particles from which it has been derived. In many respects, I am disposed to assent to this view, so long as it is not taken in too exclusive a sense. I will now, however, only mention what I consider to be its weakness. It seems to me that proof is wholly wanting as regards the statement which I have had printed in italics. That there is an enormous increase of germinal particles in the blood and in many of the tissues in these specific contagious diseases, Dr. Beale has helped to show us by his valuable researches upon the pathology of the cattle-plague and other allied affections; but that such germinal or living particles are in any direct sense the descendants of the particles which act as contagia, or, in fact, that the contagious particles really multiply to any extent in the body—these are propositions which at present appear to me to be wholly devoid of all proof. I and other pathologists are free to hold that contagious particles, whether composed of living or of not-living organic materials, may initiate changes in the tissues and fluids with which they come into contact, which changes may be exaggerated as they spread, so as at last to implicate the blood. And, as one result of this altered constitution of the nutritive fluid and of the general febrile condition simultaneously excited, we may get that undue proliferation of tissue-elements and multiplication of their products which appear to go on in the blood and in the various tissues of persons suffering from these febrile diseases.

Leaving this aspect of the question, therefore, I now turn to the special subject of this debate—viz., the truth of the germ theory, as it is ordinarily understood, or the relation of the lower organisms to virulent inflammations and their sequelæ on the one hand, and to specific contagious fevers on the other.

Applicability of the Germ-Theory to Virulent Inflammations and their Sequelæ (Gonorrhœa, Purulent Ophthalmia, Erysipelas, Hospital Gangrene, Puerperal Fever, Pyæmia, Septicæmia, etc.)—A few years ago, no one would have thought of connecting the contagiousness of gonorrhœa or purulent ophthalmia with the presence of bacteria. The respective secretions were known to contain some poisonous element either in the form of a chemical compound or altered product of tissue-multiplication (pus), which, when it came into contact with a healthy mucous membrane, was capable of acting as a specific irritant, and there exciting a similar morbid process. It is by no means certain, however, that some pathologists would not, at the present time, connect this process with the presence of bacteria in the contagious fluids. Such a point of view has, indeed, been directly fostered by doctrines recently put forward by an eminent pathologist—Dr. Burdon Sanderson. At this Society, in 1871, whilst, strangely enough, professing to be indifferent to the mode of origin of bacteria, Dr. Sanderson said: "They afford a characteristic by which we may distinguish the products of infective inflammation from those which are not infective." And in a more recent paper on "The Infective Product of Acute Inflammation" (*Medico-Chirur. Trans.*, 1873, p. 354), referring to his previous researches, he says it was inferred from these that, "if infective agents are particulate, they are probably comprised in that group of bodies to which I then applied the term micrococcytes, recognising their identity with the *zoogloea* of Cohn, the *micrococci* of Hallier, and the various forms described by other authors under the terms *bacterium* and *vibrio*". And he then adds, as the result of subsequent investigations, the following passage: "With reference to these organisms, two entirely new and most important facts have been demonstrated by the observations to be now recorded. It has been discovered (1) that, in all acute infective inflammations, micrococcytes abound in the exudation liquids; and (2) that the same forms are to be found in the blood of the infected animals". And, when Dr. Sanderson subsequently adds "that the relation of intensity between different cases of septicæmia and pyæmic infection is indicated by the number and character of these organisms", but little doubt seems to remain concerning his views as to the causal relationship of such organisms to the infectiousness of the inflammations referred to. And this view is not essentially modified by his subsequent concluding explanations, where he says: "Inasmuch as these organisms cannot have originated from the external normal tissues or juices, they must have been derived from the moisture." And, also, "It does not at all follow because these organisms come in from outside, that they bring contagium along with

them; for it may be readily admitted that they may serve as carriers of infection from diseased to healthy parts, or from diseased to healthy individuals, and yet be utterly devoid of any power of themselves originating the contagium they convey." Such a doctrine still implies that bacteria are essential to a contagious process, though it seems to me to introduce certain very striking elements of weakness into the germ-theory as thus interpreted. If this theory is not tenable, without the aid of some supplementary hypothesis, I cannot conceive that the introduction of the one above mentioned will be considered to have strengthened its foundations. Yet Dr. Sanderson apparently saw the difficulty of maintaining the germ-theory in its integrity, and offered us this other view as a compromise. He considers it probable that, whereas true contagia, whether living particles or chemical compounds, may be engendered within the body in the tissues themselves, such contagia are not able to spread either within or outside without the aid of bacteria to act as "carriers". But why one set of particles should need others to carry them, or why bacteria alone should be able to bear about these mysterious contagious poisons which they are devoid of the power of originating, does not at all appear!

However complicated the doctrine may have been rendered, this is still practically the germ-theory; and the same thing may be said with reference to a view which Professor Lister seems to entertain with some favour. He thinks that the lower fungi, and their relations bacteria, may contain in themselves some chemical compound absolutely peculiar to them, and forming part of their substance, which may act upon albuminous compounds after the manner of a ferment, such as emulsin (*Nature*, July 17th, 1873). "In this sense", he thinks, "as intervening between the growth of the organisms and the resulting decompositions, the theory of chemical ferments might be welcomed as a valuable hypothesis." This seems like the language of concession, but, practically, it is the germ-theory still, and expressed too much as all germ-theorists who think out their views would have to formulate them. It would be no great concession to those who are not believers in an exclusive germ-theory if, in the light of his views, as above expressed, Professor Lister were to say that bacteria were "carriers of infection"; yet the apparent concession above referred to is no more of a concession to believers in a physico-chemical theory than the latter admission would be.

I will, however, now briefly enumerate the evidence which seems to me quite sufficient to disprove the probability of the existence of any causal relationship between the lower organisms and the diseases cited at the head of this section, and to establish, on the other hand, the position that the bacteria met with in diseased fluids and tissues are, for the most part, actual pathological products—that they are, in fact, engendered within the body, or are descendants of organisms owning such an origin, rather than of previously existing organisms introduced from without. It would take far too long were I to attempt to enter at any length upon a consideration of this evidence. I must, therefore, content myself with briefly summarising the principal facts and arguments on which a judgment may be founded.

1. The experiments of many investigators prove that the alleged causes of disease may be actually introduced into the blood-vessels of lower animals by thousands without producing any deleterious effects in a large proportion of the cases.

2. Bacteria, if not actually to be found within the blood-vessels of healthy persons, do nevertheless habitually exist in so many parts of the body in every human being, and in so many of the lower animals, as to make it almost inconceivable that these organisms can be causes of disease. In support of this statement I have only to say, that even in healthy persons they may be found in myriads in and about the epithelium of the whole alimentary tract from mouth to anus; they exist throughout the air-passages, and may be found in mucus coming from the nasal cavities, as well as in that from minute bronchi. They exist abundantly amongst the epithelial *débris* within the ducts of the skin, not only in the face, but in other parts of the body. Fresh legions of them are also being introduced into the alimentary canal with almost every meal that is taken, whence they may perhaps readily find their way into the mesenteric glands, if not further within the system. And lastly, in persons with open wounds, bacteria are constantly to be found in contact with such surfaces, especially if the wounds be not well cared for, though the injured person does not necessarily suffer at all in general health.

3. It is no answer to these difficulties to say that there are distinct species amongst these lower organisms, some of which are harmless, though others are poisonous (or so-called "germs" of disease). In support of such opinion, nothing can be alleged save some of the facts whose cause is doubtful; whilst against such an interpretation may be brought the experiments of several investigators, showing that bacteria are the creatures of circumstance, and modifiable to an extraordinary

degree. The last position is even admitted by Professors Sanderson and Lister. The former acknowledges that they are "the lowest organisms," and that they are "much more under the influence of the conditions under which they originate and are developed than organisms of any other class", whilst Professor Lister's own work has compelled him to make an admission which, in the face of facts previously stated concerning the wide distribution of bacteria within the body, seems fatal to a consistent belief in the germ-theory of disease. He says: "If the same bacterium may, as a result of varied circumstances, produce in one and the same medium fermentative changes differing so widely from each other as the formation of lactic acid and that of black pigment in milk, it becomes readily conceivable that the same organism which under ordinary circumstances may be comparatively harmless, may at other times generate products poisonous to the human economy."

—(*Quart. Jour. of Microscop. Science*, October 1873.)

4. The consideration now to be mentioned suffices, in my opinion, to complete the discomfiture of the germ-theory as an explanation of the mode of causation of the diseases with which we are at present concerned. It is this. It has been shown, on the one hand, that the virulence of certain contagious mixtures diminishes in direct proportion to the increase of bacteria therein; and on the other hand, it has been equally proved that fresh and actively contagious menstrua lose scarcely any of their contagious or poisonous properties after they have been subjected for a few minutes, when in the moist state, to a temperature which no living units can be shown to survive (212 deg. F.), or after they have been exposed to the influence of boiling alcohol, which is well known to be equally destructive to all recognised forms of living matter. Such facts have been substantiated by Messrs. Lewis and Cunningham, Sanderson, and others.

Having said thus much in opposition to the germ-theory, let me as briefly enumerate the facts and arguments which seem to me to show the real relations of bacteria and their allies to the diseases in question. I turn, therefore, to the construction of an opposite doctrine.

Admitting in part the very frequent presence of bacteria in diseased fluids and tissues, I consider that their presence and import should be differently explained. I say I admit the association in part, though I by no means admit it to the extent alleged. Bacteria are not, for instance, to be found in the blood of persons suffering from pyæmia, as might be inferred from former statements of Dr. Sanderson, which I have already quoted. My own experience in this matter seems to be entirely in accordance with that of Professors Billroth and Stricker. Neither do I believe that the presence of bacteria in inflammatory fluids has the significance which Dr. Sanderson attaches to it, since it has been ascertained by myself and others that the exudation-fluids of sick persons suffering from diseases of a totally different type, are often similarly crowded with these lowest organisms; whilst the recent observations of M. Bergeron (*Compt. Rend.*, February 1875) seem to show that they may be found even in freshly extracted pus from ordinary abscesses occurring in elderly persons.

Now, it would seem quite obvious, that the consistent advocate of a germ-theory of disease can only successfully maintain such a doctrine if he can show, amongst other things, that bacteria are more capable of altering the characters and chemical constitution of fluids of the body than they are themselves prone to be altered by independently initiated changes taking place in such fluids. It seems, therefore, like unintentionally cutting himself free from the theory to which he has hitherto adhered, when we find Professor Lister, in speaking of the assumed "special virus of hospital gangrene", going on to say that "it is not essential to assume the existence of a special virus at all, but that organisms common to all the sores in the ward may, for aught we know, assume specific properties in the discharges long putrefying under the dressings". This passage has a similar import to that of a quotation previously made. In both, a first place is assigned to the modifying influence of altered fluids; and, however much the correctness of such a supposition would tell in favour of cleanliness, of free exposure, or even of antiseptic dressings, it is none the less inimical to a consistent holding of the theory on which Professor Lister has chosen to base his system of treatment.

But, though such statements are adverse to the holding of a germ-theory in the only form in which it may be at all tenable, they are entirely in accordance with my own observations and views. I maintain, in short, that even the very existence of organisms in the fluids and tissues of diseased persons is for the most part referable to the fact that certain changes have previously taken place (by deviations from healthy nutrition) in the constitution and vitality of such fluids and tissues, and that bacteria and allied organisms have appeared therein as pathological products—either by heterogenesis, or by what I have termed archebiosis, or birth direct from a fluid.

The evidence on which my belief is founded is of this nature.

1. Bacteria and their allies are found in greatest abundance during the life of the individual in connection with dying tissue-elements, and apparently are as plentiful within the dying epithelium of the cutaneous ducts, as in parts like the mouth, which are most liable to contamination with organisms from without. Again, they exist abundantly in and about the dying cells of bronchial mucus, although living bacteria appear to be almost completely absent from ordinary air.

2. The microscopical examination of such epithelial or mucous elements also favours the notion that the contained bacteria are products engendered within such cells, rather than mere results of an external contamination and imbibition. This opinion is based upon the following considerations. Bacteria only appear within the cell when it is obviously dying; and, in the case of epithelium, for instance, they manifest themselves at first as minute motionless particles scattered through the semisolid substance of the cell, where each particle grows into a distinct bacterium, which still remains motionless, and does not appear to divide for a long time. This is precisely similar to what I have observed over and over again, when amœbæ in vegetable infusions grow into an unhealthy condition and become resolved into nests of bacteria. They may exist for days in a state of activity with bacteria in the fluid around them, though none are to be seen in their interior. After a time, however, the chemical constitution of the fluid seems to become no longer suited to the amœbæ, their activity ceases, they remain as almost motionless balls of jelly, and soon multitudes of the minutest particles appear throughout their substance, each of which straightway grows into a bacterium. The former amœba is converted into a mere bag of bacteria, which after a time ruptures, and thus liberates its swarming colony of newly engendered living units. Multitudes of mucus-corpuscles seem to undergo the same kind of change, so that bacterial degeneration takes place in the same manner, and is almost as typical amongst them, as is fatty degeneration amongst pus-corpuscles. The two kinds of degeneration, moreover, commonly occur side by side in epithelial debris. Bacterial degeneration takes place where the vitality of the unit is lowered, but where it is not sufficiently degraded to permit the still lower and more obviously destructive process of fatty degeneration; and if anyone wishes to see it in perfection, let him examine some central portion of the kidney, or other internal organ of a warm-blooded animal, five days or more after its death.

3. Bacteria are admitted by nearly all pathologists to be absent from the blood of healthy persons during life; and yet, in from eight hours to four or five days after death, according to the temperature of the air at the time, the previously germless blood of all individuals may be found to be swarming with these organisms in every stage of growth.

4. Whereas blister fluid or serum has been shown to be free from organisms in healthy persons, I have ascertained that, given a febrile patient with a temperature of 102 deg. Fahr., one can determine the presence of bacteria, at will, in any blister-bleb which remains intact for forty-eight hours or more, and this, too, where the patient does not suffer from any specific fever, but merely from pneumonic inflammation. I was led to ascertain this fact by finding, about eighteen months ago, myriads of bacteria in all the blebs of a patient suffering from acute pemphigus, with a temperature of 103 degs.

5. Lastly, as Dr. Sanderson has shown, a chemical irritant, such as liquor ammoniæ, may be introduced beneath the skin of some of the lower animals in such a way as to "preclude the possibility of external contamination", and yet here, amidst tissues which he has shown to be germless, we may thus, within twenty-four hours, determine the presence of swarms of germs and organisms in the pathological fluids effused under the influence of the local chemical irritant.

This constitutes, as it appears to me, an exceedingly strong body of evidence tending to show that bacteria are pathological products capable of being engendered within the body after death, or in certain situations during life where tissue-elements are dying, or where the fluids of the body are notably altered by disease. It is true that the facts and considerations mentioned under 1 and 2 are capable of receiving another interpretation. It may be said, for instance, and it has actually been said by Dr. Beale, that the higher forms of life are, as it were, interpenetrated by the lower forms of life. Speaking of bacteria and their allies, Dr. Beale says:—"I have detected them in the interior of the cells of animals, and in the very centre of cells, with walls so thick and strong, that it seems almost impossible that such bodies could have made their way through the surrounding medium." (*Disease-Germs*, page 72, 1870.) And elsewhere the same observer says:—"Probably there is not a tissue in which these germs are not; nor is the blood of man free from them." Noting by the way that this latter statement does not accord with the experience of others, I may further mention that some distinguished pathologists, and notably

Dr. Burdon Sanderson, are also inclined to dwell strongly upon the fact of the wide distribution of bacteria throughout the body—not believing them to be innate or connate (in the mysterious manner imagined by Dr. Beale), but supposing that they have been introduced from without through certain definite channels.

Dr. Sanderson's views on this subject, and the means by which he supports them, are sufficiently remarkable to detain us a few moments. If what he says (BRITISH MEDICAL JOURNAL, February 13th, 1875) concerning the assumed easy absorption of bacteria from the intestine by lymphatics, and their subsequent passage into the blood, were in correspondence with actual facts, then, in face of the habitual prevalence of such organisms in the intestine, the blood of healthy individuals should scarcely ever be free from them. But this is surely proving too much, since Dr. Sanderson himself assures us that healthy blood is germless.

Again, the other main channel by which, as he says, bacteria may enter into the body abundantly from without, is through the bronchi and the lungs. Now, as a result of Dr. Sanderson's oft-quoted experiments in 1871, he claims to have proved "in the most striking manner . . . that air is entirely free from living microzymes". Speaking of a previously boiled Pasteur's solution, he says that "no amount of exposure" to air "has any effect in determining the presence of microzymes therein". And yet Dr. Sanderson now talks of the air which is "entirely free from living microzymes" being the channel through which these organisms are introduced into the lungs. It is true that, in his recently published lectures, this distinguished investigator makes a tacit retraction of his previous statement. He says, in fact, in his first lecture (BRITISH MEDICAL JOURNAL, January 16th, 1875):—"It must not be understood that bacteria do not exist in the atmosphere. But their existence there in an active form strictly depends on moisture. They attach themselves without doubt to those minute particles which, scarcely visible in ordinary light, appear as motes in the sunbeam or in the beam of an electric lamp. It is by the agency of these particles that they are conveyed from place to place." Elsewhere, in the same lecture (page 70), Dr. Sanderson repeats the statement, that "solid materials in suspension in the air" play a principal part in the conveyance of bacteria from place to place, and alleges that this was shown by the very experiments of 1871, which then entitled him to express the conclusion that "air is entirely free from living microzymes". All I can say is, that I have not been able to find in Dr. Sanderson's writings any explanation of this marked change of view, and that I certainly know of no experiments of his which at all establish the fact (extremely difficult as it would be to establish) that bacteria or their germs are conveyed from place to place on the surface of aerial particles, just as his assumed particles of contagium are supposed to be borne about by bacteria themselves. If the theory be true, the conditions for aerial locomotion of contagia are, at all events, becoming a little complicated. The contagious particles cannot move about alone; they must engage the services of bacteria to carry them, and these latter porters are unfortunately so delicately constituted, that they cannot exist alone in the atmosphere; they can only survive when borne on the backs of some moisture-containing fragments of atmospheric dust, which, though much heavier than the contagious particles themselves, are freely borne through the air in all directions.

Turning from these statements, therefore, as to the assumed modes by which bacteria habitually gain an entry into the healthy human body, I may say, that many of the methods by which Professor Kühne, Dr. Sanderson, and others (BRITISH MEDICAL JOURNAL, February 13th, p. 199), have attempted to ascertain whether the different tissues contain actual or potential germs, are pointless in the face of the statements of heterogenists; since their methods cannot enable them to say, when positive results are obtained, that the potential germs from which, as they assume, the organisms have been developed are other than elementary particles of the previously healthy, though now altered, tissues, or that they have not been produced from the fluids which the tissues contain. These experimental observations are not only almost valueless on this account, but they are altogether needlessly complex. Why resort to heated knives, boiled thread, rapid movements, frequent immersions in paraffin at 260 deg. Fahr., paper boxes, warm chambers, etc., when precisely similar results might be obtained by simply leaving the dead animal alone for three or more days, and then subjecting the central tissues of either of the viscera to microscopical examination? So far as the principle of the method is concerned, or the kind of results which it may yield, it makes no difference whether we keep an extracted portion of tissue enveloped in paraffin in a warm chamber for hours or days, or resort to the much simpler method of leaving the animal unopened for several days before submitting its tissues to examination. In either case where organisms are found, this fact alone would give us no right to infer that they had developed from

pre-existing germs (in the natural history sense of that term); they may, on the contrary, have arisen either by heterogenesis or by archebiosis.

The weight of probability in favour of either of these two possibilities can only be judged of by resort to a different method of procedure; because, in view of the observed absence of bacteria from the tissues of such organs as kidney, liver, or brain, immediately after death, the subsequent multitudinous presence of organisms in these situations would, in the face of satisfactory independent evidence, be more easily accounted for by heterogenesis or archebiosis than by the hypothesis of pre-existing latent or potential germs. By an appeal to evidence of this kind, moreover, we are enabled to test the probability of the hypothesis previously referred to as being supported by Dr. Beale and others—viz., that which assumes the existence of invisible and mysteriously derived germs of bacteria and fungi throughout the elements of the tissues—an hypothesis somewhat wild in character, which has, I believe, no other foundation than the frequently observed prevalence of organisms in some of these situations.

With the view of settling these questions, therefore, we may carefully prepare an infusion from some animal tissue, be it muscle, kidney, or liver; we may place it in a flask whose neck is drawn out and narrowed in the blow-pipe flame; we may boil the fluid, seal the vessel during ebullition, and, keeping it in a warm place, may await the result, as I have often done. After a variable time, the previously heated fluid within the hermetically sealed flask swarms more or less plentifully with bacteria and allied organisms, even though the fluids have been much degraded in quality by exposure to this high temperature, and have thereby, in all probability, been rendered far less prone to engender independent living units than the unheated fluids in the tissues would be. We operate, however, under these disadvantageous conditions in order to make thoroughly sure that, by the preliminary heating, we have destroyed all pre-existing life within the flask; and, notwithstanding such adverse circumstances, we are able to obtain evidence of the occurrence of archebiosis. The researches of Kühne and others have fully shown that the protoplasm entering into the composition of the tissues of warm-blooded animals is coagulated and killed at a temperature of 111 deg. Fah.; whilst my own investigations (*Evolution and the Origin of Life*, 1874, page 101) also show that bacteria and allied organisms are killed by exposure in the moist state to a temperature of 140 deg. Fah.

Hence I contend that the wide distribution of bacteria throughout the human body in connection with dying tissue-elements in the most varied situations, and also in diseased fluids, is explicable most easily by assigning for many of them an origin by heterogenesis and by archebiosis (though when so produced they multiply rapidly in the ordinary fashion); and that my position—that bacteria are pathological products—is one which may claim to have been fairly established.

On this subject I would only add a word or two concerning the point of view and reasoning employed by those who seem willing to believe in almost any infringement of natural uniformity, rather than admit the occurrence of heterogenesis and archebiosis, or either of them alone. The most remarkable recent utterances on this subject are those of Dr. Sanderson, though it is only fair to say that they are somewhat typical of the line of argument adopted by many others.

Whilst admitting that bacteria in their "ordinary state" have been proved to be killed at a temperature of 140 deg. Fah., and also by immersion in absolute alcohol, Dr. Sanderson assumes (BRITISH MEDICAL JOURNAL, February 13th, page 201) that other bacteria-germs may exist in an extraordinary state in which they have the power of resisting the influence of this temperature, the influence of absolute alcohol, and even the simultaneous action of both these destructive agents. But, if we ask on what amount of evidence this assumption is founded, many may be astonished to find that such an extraordinary belief has been adopted, simply because bacteria make their appearance in an organic infusion which has been prepared by macerating an organic extract previously submitted to the influences above mentioned, just as bacteria make their appearance within our closed flasks whose contents have been previously heated to the higher temperature of 212 deg. Fah. Has it ever occurred to Dr. Sanderson that another interpretation might have saved him from the necessity of adopting this extraordinary belief?

Again, in his third lecture, the same investigator shows himself for the time similarly oblivious of the point of view of those who believe in archebiosis, whilst the argument made use of to support his own position is of a very surprising nature. After remarking (BRITISH MEDICAL JOURNAL, March 27th, p. 403) that "of all perishable things, protoplasm is amongst the most perishable", he goes on to state that bacteria possess "a wonderful property of passing into a state of persistent inactivity or latent vitality". This is nothing more than an explicit expression of the notion previously referred to, though I wish especially to call attention to the additional "evidence" upon

which the view is now based. Dust, containing organic *débris*, in which, as Dr. Sanderson confesses, he has no proof that anything living is contained, may be added to a fluid at the time barren, though freely capable of supporting life. One of the results of this addition is the appearance, after a short time, of bacteria. A physicist or chemist might conceive it possible that, as a consequence of such admixture, a compound not previously existing might have been more or less slowly formed—as this, at all events, is one of the modes by which new chemical compounds are engendered. But this point of view Dr. Sanderson will not seriously entertain—indeed, his remarks seem only explicable from the point of view of a foregone conclusion that archebiosis is an impossible process, and therefore on no account to be admitted as an interpretation of the facts. In reply to an imaginary objection, alleging that he had no proof that the dust contained anything living, he says with great *naïveté*:—"True; but I have proof that it contains that which produces life, and express this state of things, viz., the absence of manifestations of life on the one hand, and on the other the fact that the stuff in question possesses the power of impregnating something else which before was barren, by saying that the dust possesses latent vitality". The legitimacy of the inference does not seem very apparent to me, if it is to be taken in any other than a poetical sense; yet this is the only evidence adduced in favour of the assumed existence of an extraordinary state in which bacteria may exist—a state in which they are assumed to be capable of resisting influences which are admitted to be destructive to all actually known forms of life. Of course, on the same grounds, the physicist might argue that "friction possesses latent electricity", or the chemist that "oxygen possesses latent acidity", but it seems very questionable whether such statements would be regarded as serviceable additions to science. Neither can we consider that any further light is thrown upon this notion of "latent vitality" by Dr. Sanderson's concluding observations upon the subject, in which he says (BRITISH MEDICAL JOURNAL, April 3rd, p. 436):—"The vital activities of the organism are stored up for the future, *the individual being for this very end endowed with the power of resisting external agencies, and thereby of enduring for an indefinite period*". As to such teleological notions I have nothing to say; I prefer keeping to the region of fact and warranted inference. These, however, are the arguments by which a belief in the occurrence of archebiosis and heterogenesis is for the time averted.

Before drawing my remarks on this section of the subject to a close, I would point out that the views admitted by Dr. Beale and those who think with him, those admitted by Dr. Sanderson, Professor Kühne, and Dr. Tielgel, as well as those recognised by myself and others, all coincide with one another on a certain common ground. We are agreed as to the fact that bacteria are abundantly present within the body, or that they may appear therein under certain conditions independent of any immediate external contamination—however much we may differ amongst ourselves as to the interpretation of their presence, actual or possible. Yet this common ground contains an admission which is decidedly inimical to Mr. Lister's theories. Following M. Pasteur, this distinguished surgeon would have us believe, that whilst bacteria are disease-germs, they do not naturally exist within the body. He has based his antiseptic system of treatment on the assumption that air, or surfaces which have been exposed to it, coming into contact with wounded portions of the body, are the means by which his assumed animated poisons are introduced into the system. But it is, I think, now well known that the whole pyæmic process may be met with occasionally, even where there is no abrasion of the surface of the body. And, moreover, as regards the cause of the disease in persons with open wounds, I may say that Pasteur never seriously attempted to discriminate between the respective effects of the living and the dead elements entering into the composition of atmospheric dust. Effects which were often due to the action of mere organic *débris* he attributed to the influence of living germs (*Evolution and the Origin of Life*, pages 103-114); and in this respect M. Pasteur has been followed by Professor Lister.

But, as I take it, the essential practical fact which Professor Lister wishes to enforce is, that the putrefactive processes apt to take place in wounds ought to be reduced to a minimum, because it seems certain that, during such processes, poisons are liable to be engendered whose absorption or local influence upon the system may be attended by the most fatal results. Such a notion, which is assuredly thoroughly well founded, may, however, be acted upon by the adoption of the antiseptic system of treatment (or by free exposure of wounds and frequent removal of secretion), quite independently of the question whether mere organic *débris* may act as ferments, and also quite independently of the further question whether the poisons engendered in wounds are living entities or complex chemical compounds not endowed with the attributes of living matter.

Applicability of the Germ-Theory to Artificial Tuberculosis, Syphilis, Typhoid, Typhus, Relapsing Fever, Cholera, Measles, Scarlet Fever, Small-pox, and other Contagious Fevers.—I now pass to a consideration of the germ-theory in its relation to another class of diseases, although I do not wish to convey the idea that there exists in nature a distinct boundary line, such as my division of the subject might indicate. It must be clearly understood, that the local morbid processes or inflammations of a virulent type—which may or may not gradually entail a more general morbid condition—pass insensibly, by means of such affections as artificial tuberculosis and syphilis, into that class of diseases under which are included such affections as typhus, typhoid, relapsing fever, cholera, measles, scarlet fever, small-pox, and other contagious fevers. Affections like artificial tuberculosis and syphilis might, therefore, have been placed with equal appropriateness in either of the divisions I have adopted.

The treatment of the present part of my subject may be disposed of in a more summary manner than the last, principally because many of the facts and considerations which were advanced in reference to virulent inflammations and their sequelæ, and the presence of independent organisms in the altered fluids and tissues of the body, are also applicable to the question of the relation of such organisms to the more specific contagious fevers.

The case to be made out in favour of the germ-theory, as applied to these latter fevers, is also, in my opinion, much weaker than it is in respect to the virulent inflammations and their sequelæ; since, although such contagious fevers have always been regarded as general and essentially "blood-diseases", in only one of those occurring at all commonly in the human subject does it appear that anything like an independent living organism is to be met with in the blood. There is, therefore, here a *primâ facie* inherent weakness in the whole theory, which I think a thorough examination of the question will strongly tend to confirm, rather than dissipate.

The reasons relied upon in favour of the germ-theory, as applied to these diseases, are of a purely *à priori* or theoretical nature, and such as I have already referred to. They are, in fact, based upon the assumed nature of contagium, and upon its assumed mode of increase within the body. How little conclusive such *à priori* reasons are, and how the facts may be otherwise explained I have already endeavoured to show, and as the theory in its applicability to these diseases rests upon absolutely no positive evidence that I am aware of, I am compelled to leave a gap here, and pass on to a brief enumeration of the facts and considerations which seem to tell strongly against the existence of any causal relationship between organic germs and these specific contagious fevers.

1. With two exceptions, no definite germs or organisms are to be met with in the blood of patients suffering from these diseases during any stage of their progress.
2. The virus or contagium of some of these diseases, whatever it may be, does not exhibit the properties of living matter.
3. On the other hand, the virus or contagium of most of these contagious diseases with which definite experiment has been made, is most potent in the fresh state, whilst its power very distinctly diminishes in intensity as organisms reveal their presence more abundantly therein—facts which would seem to point to the conclusion, or at least are quite consistent with the notion, that the contagious poison may be a chemical compound which gradually becomes destroyed or modified by the successive changes taking place in association with processes of putrefaction.
4. There is the extreme improbability of the supposition that this whole class of diseases should be caused by organisms known only by their effects.
5. The facts of the sudden cessation, periodical visitation, and many of the other phenomena of epidemics, however difficult they may be to explain upon any hypothesis, seem to oppose almost insuperable obstacles to the belief that living organisms are the causes of such epidemics of specific contagious diseases.

It would seem little better than an ill-timed attempt at jesting to postulate the existence of distinct germs for these several specific fevers, and at the same time to endow such imaginary entities with properties different from those of all known germs. To remain always in the germ stage in media favourable for their multiplication would, even if the imaginary germs were visible, be contradictory to all previous experience; but to suppose, in addition, that such hypothetical invisible entities are capable of resisting the influence of agencies which have been proved to be destructive of all known living matter, would seem to be going altogether beyond the bounds of probability. And, if we look at the question from this point of view, we may regard it as a definitely established fact that the virus of cholera, for instance, is not composed

of living germs or particles. Messrs. Lewis and Cunningham have shown (*Report, etc., into the Nature of the Agent or Agents producing Cholera*, pp. 46 and 57, 1874) that the virus is not appreciably impaired in activity when the fluids containing it have been raised for a few minutes to a temperature of 212 deg. Fahr.; and, in reference to this subject, they say: "We have seen no living object preserve its vitality after exposure in a fluid to a temperature approaching to 212 deg. Fahr., nor have we been able to satisfy ourselves that anyone else has done so."

In only one of the specific fevers commonly met with in the human subject have organisms been found in the blood: this exception is relapsing fever. There is, however, an affection occasionally communicated from cattle (*sans de rate*, or splenic fever) in which organisms are occasionally met with in the same situation. But the fact of the existence of actual visible organisms in these cases seem altogether robbed of its significance, after the occurrence of archebiosis and heterogenesis in diseased fluid and tissues has been demonstrated. The view, indeed, that the organisms found in these affections owe their origin to certain changes prone at times to occur in the fluids of the body, is directly supported by some of the most interesting results of Dr. Sanderson's experiments concerning pyæmia. He tells us that in some of the lower animals artificial tuberculosis and pyæmia are often only different effects of the same cause. That is, that some of the same inoculating material may be introduced beneath the skin of two rabbits, and in the one a slow and more chronic set of morbid changes is induced (tuberculosis), whilst in the other more acute and rapidly fatal processes are established (pyæmia). In the former animal no organisms are to be found in the blood, whilst the blood of the latter, according to Dr. Sanderson, is swarming with them. Changes in the character of the morbid process, therefore, may occasionally favour the presence of organisms. Nay, further, we see the same kind of difference in another way. Pyæmia and septicæmia, as they occur in some of the lower animals, differ in one very notable respect from the same diseases as they occur in man. Whilst in the lower animals bacteria are to be found in the blood of the living animal, in man they are always absent during life. With such facts as these before us, and others previously referred to concerning the absence and presence of organisms in blister-fluid from different individuals, it need not excite much surprise if we find that organisms are to be found in the blood of persons suffering from one or more of these specific contagious fevers.

There are, however, three other diseases of this class in which organisms, though absent from the blood, are to be met with in those parts of the body which are severally the special seat of morbid change. The three diseases are—vaccinia, ovine small-pox (which seems to be altogether similar to the disease occurring in man), and typhoid fever.

That the organisms of the vaccine vesicle have any significance other than from being possible instances of heterogenesis or archebiosis, I find it difficult to believe. Even if the contagious property of the fluid be resident in some of its particles, as the observations of M. Chauveau and Dr. Sanderson seem to prove, still such particles may exist and yet not be the independent organisms existing in the same fluid. The fact that as the organisms increase in the fluid with age the virus loses its intensity, and the fact that it may remain potent even after prolonged periods of desiccation, are both of them strikingly opposed to the notion that the living organisms of the fluid are its active elements in a specific sense. On the other hand, it does appear, from the experiments of the late Dr. Henry, of Manchester, that vaccine virus loses its intensity when subjected to a temperature of 140 deg. F.

In ovine small-pox we have, as Dr. Klein's very interesting researches have shown (*Proceedings of the Royal Society*, No. 153, p. 1874), a local appearance and active growth of organisms taking place in the skin in connection with its characteristic pustules; whilst in typhoid fever we have also an active growth of rather different organisms in the substance of the ileum, and more especially in the tissues constituting Peyer's patches—that is, in connection with the anatomical marks of this disease. (BRITISH MEDICAL JOURNAL, December 5, 1874.) But just as a mere chemical irritant (ammonia) injected beneath the skin of a rabbit produces, as Dr. Sanderson tells us, a local inflammation in which the fluids effused swarm with bacteria, why may not the morbid processes taking place within the skin in small-pox engender irritants which may lead to the appearance of somewhat similar products? Hence, in face of the evidence already detailed concerning the occurrence of heterogenesis, the presence of organisms in connection with small-pox lesions may be readily accounted for, without the necessity of attaching any very important rôle to them. And as regards the presence of organisms in Peyer's patches and adjacent parts, in cases of typhoid fever, no greater importance could be accorded to this association by any but enthusiastic germ-theorists. For, even if the reasons above alluded to

were not very influential with them, there is another mode of looking at the matter, from quite an orthodox point of view, which would equally assign to the local development of organisms a very subordinate rôle. Morbid tissues are generally admitted to form a favourable nidus for fungoid growths, and the intestine is known to contain the germs or spores of such bodies. The flourishing growth of leptothrix and fungi in the diseased mucous membrane may therefore be only another example of an already well-known class of effects; so that, looking at the question from all sides, it seems to me, in the present state of our knowledge, to be extremely improbable that these newly discovered organisms have any causal relationship to typhoid fever.

It only remains for me now to make a few very brief concluding observations—(1) concerning Pasteur's recent important modifications of his germ theory of fermentation; (2) upon the degree of relationship existing between fermentation and zymosis; and (3) as to the probable mode of action of ferments and contagia.

I. Pasteur has, within the last two years, made a most important modification in his theory of fermentation (*Compt. Rend.* 1873-4). Whilst he formerly held that fermentation and putrefaction are chemical processes initiated by independent organisms (bacteria and their allies), and taking place in correlation with their growth and multiplication, he has of late shown that similar phenomena may be initiated by the chemical processes taking place in the tissue-elements of certain fruits and vegetable tissues, when these are placed under certain abnormal conditions. Grapes, for instance, suspended in an atmosphere of carbonic acid, will undergo fermentation, so as to generate alcohol and other products, even without the presence of torulæ or allied organisms. Other fruits and vegetables treated in the same way behave more or less similarly. Organic multiplication of independent organisms has therefore now been shown, by Pasteur himself and his followers, not to be an essential factor in the process of fermentation. With this admission, I believe it will be found impossible hereafter consistently to entertain an exclusively "vital" theory of fermentation, and equally impossible to resist accepting the broader physico-chemical theory, and with it the almost inseparable correlative doctrines of archebiosis and heterogenesis.

M. Pasteur, in fact, now proves that fermentation takes place under the influence of altered chemical (nutritive) processes taking place in unhealthy vegetal tissue, just as we know that similar processes may be initiated under the influence of a physico-chemical process brought about by finely divided platinum. As Döbereiner pointed out, this material "has the power—and many organic substances have a similar power—of absorbing oxygen from the air, and bringing it into a condition in which it can unite with other substances with which it would not otherwise enter into combination at low temperatures" (*Beginnings of Life*, vol. i., p. 409).

And MM. Lechartien and Bellamy, following up the recent experiments of Pasteur, have found (*Compt. Rend.*, November 2, 1874) that in these modified processes of fermentation, taking place in vegetal tissues, independent organisms, though they are usually absent at first, not infrequently make their appearance after a time. In the process as it occurs in beetroot and in the potato, on the other hand, bacteria habitually spring into existence or reveal themselves in great abundance soon after the commencement of a well-marked process of fermentation. M. Pasteur will, I suspect, find it difficult consistently to account for these facts, without admitting his long-postponed acceptance of doctrines of "spontaneous generation".

2. Respecting the degree of relationship existing between fermentations and zymotic processes, something more definite may now be said. Between the ordinary, previously known forms of fermentation, and zymosis, a most fundamental difference exists, which has hitherto been far too much lost sight of. It is this. Whereas in an ordinary fermenting fluid the changes initiated by a ferment take place in a mere isolated mixture of organic substances, in zymotic processes the changes initiated by contagium occur in the fluids and tissues of a complex living body. That this latter fact does exercise a very important influence, and that the two processes are not so similar as they have been supposed, we may now more readily recognise, since the processes of fermentation occurring in vegetal tissues have been investigated. The relationship existing between zymosis and these modified processes of fermentation taking place in fruits and tubers seems, indeed, far more close than that between the zymotic processes in animals and ordinary kinds of fermentation.

In the process-occurring in vegetal tissues, as well as in those morbid processes which take place in the animal organism, the presence of rapidly multiplying independent organisms is an occasional rather than a necessary feature. Though usually absent in other allied processes, yet do we find organisms invariably manifest themselves throughout

the tissues of beetroot and of the potato, when these are placed under certain abnormal ("unhygienic") conditions. And, though usually absent from the blood of persons suffering from specific contagious fevers, yet do we also find organisms invariably showing themselves in the blood of persons suffering from some of them—such as relapsing fever and splenic fever. Nay, further, under the influence of a "change of conditions" alone, we may initiate these modified fermentative processes in vegetables—that is to say, in ordinary parlance, the processes may originate "spontaneously" or *de novo*. But if the modified activity of tissue-elements suffices to initiate such morbid processes in the vegetal organism, why may it not occasionally do the same in the animal organism? This is a point of view which seems too valuable to be lost sight of, more especially in the face of the results yielded by our flask experiments.

3. In conclusion, I would maintain that the facts already known abundantly suffice to displace the narrow and exclusive vital theory, and to re-establish a broader physico-chemical theory of fermentation.

Whether the "ferment" in any given case be an independent living organism, a tissue-element, a fragment of not-living organic matter, or some mere physico-chemical influence (as in the case of the action of finely divided platinum), the initiative fermentative change is in each case a result of chemical action. And similarly, with regard to "contagium", whether it be an altered though living tissue-element, a fragment of dead organic matter, a chemical compound (or even the more vague influence of a "set of conditions", which may suffice to generate contagium *de novo*), we have in each case to do with gradually initiated chemical changes, distinctive in kind, and gradually terminating in one or other of the recognised varieties of zymotic affections. The changes in each case where we happen to have to do with living ferments or living contagia would be due only to an infinitesimal extent to the organic multiplication of such living units, though the decompositions set up by them in their respective fluids may be such as to lead to the formation of a continuous new birth of independent organisms, all of which exhibit most active powers of multiplication. The organisms produced in such cases are, therefore, only to an infinitesimal extent lineal descendants of the original living ferments or contagia, under whose influence such fermentative or zymotic processes were originally established. (*Beginnings of Life*, vol. ii., p. 361.)

Thus it would appear that the original notion borrowed from the vital theory of fermentation, that all the organisms met with in a fermenting mixture are in the strict sense of the term lineal descendants of those originally introduced as ferments, would disappear with the vital theory itself. Yet this has been the notion upon which upholders of the germ-theory of disease have always relied confidently, in explanation of the mode of increase of contagium within the body.

Looking, however, at this question from our new point of view, may we not say that chemical changes established in some one tissue, or in many, may, by dint of altered blood and other secondary processes, spread so as to be initiated also in previously sound parts; and that thus throughout the body, or in some special regions of it, living tissue, endowed with peculiar poisonous properties, or complex alkaloidal compounds, may be engendered in enormous quantities, some of which may be thrown off from this or that surface, and act after the fashion of "contagia" generally.

THE TEMPERATURE IN PHTHISIS.

SHORTLY after the publication of Dr. Sidney Ringer's work on the *Use of the Thermometer in Phthisis*, I made a number of thermal observations on phthisical patients, and came to the conclusion that valuable as the thermometer is in the diagnosis of a variety of diseases, yet, as a test of the deposition of tubercle, it is unreliable. In cases of incipient phthisis, with obscure physical signs, it did not aid the diagnosis; it was unsafe to say that there was no disease because the temperature was normal. In many cases, there was no rise, yet signs of tubercular deposit gradually unfolded themselves. In others, a rise of two or three degrees occurred, but often there was slight bronchial inflammation which might account for it. In more advanced cases, there was of course softening, and often subacute pneumonia, bronchitis, etc. I believe that the thermometer indicated only the pyrexia produced by these complications. Subnormal temperature was occasionally observed when the vital powers were low. I several times intended to record these observations, but feared they were not sufficiently elaborate to satisfy the profession, although they convinced me. Dr. Theodore Williams has now more efficiently done so; and it is satisfactory to find his conclusions tally with mine.

H. STRANGWAYS HOUNSELL, M.D., M.R.C.P. Lond., Physician to the Western Hospital for Consumption, Erith House Institution, etc., Torquay.

ON THE ACTIONS OF PICROTOXINE, AND THE ANTAGONISM BETWEEN PICROTOXINE AND CHLORAL HYDRATE.

By J. CRICHTON BROWNE, M.D., F.R.S.E.,
Medical Director of the West Riding Asylum.

(Continued from page 444.)

CERTAIN conclusions having thus been arrived at as to the actions of picrotoxine and as to the toxic symptoms produced by it when uninterfered with by treatment, it became necessary in the next place to ascertain accurately the minimum fatal dose of it, in those animals which it was proposed to make use of, in testing the supposed antagonism between it and chloral hydrate. The results of the experiments which were performed with this view are shown in the two following tables.

TABLE II.—Showing the Minimum Fatal Dose of Picrotoxine in Rabbits.

No.	Weight of Rabbits.	Dose of Picrotoxine in parts of a grain.	Effects.	Result.
9	2 lbs. 6 oz.	1-60th	Dulness, hurried breathing, and prostration	Recovery
10	3 lbs. 2 oz.	1-40th	Lethargy and unsteadiness in movements	"
11	3 lbs. 2 oz.	1-30th	Dulness, quickened respiration, restlessness, twitching of ears	"
12	3 lbs. 7 oz.	1-25th	Lethargy, hurried respiration, twitchings.	"
13	3 lbs. 9 oz.	1-25th	Prostration, hurried respiration, severe twitchings	"
14	3 lbs. 3 oz.	1-20th	Lethargy, restlessness, violent convulsions	Death in 84 min.
15	2 lbs. 12 oz.	1-20th	Dulness, twitchings, violent convulsions	Death in 75 min.
16	3 lbs. 3 oz.	1-8th	Lethargy, hurried breathing, trembling, violent convulsions	Death in 32 min.
17	2 lbs. 2 oz.	1-3rd	Drowsiness, twitchings, violent convulsions	Death in 30 min.
18	2 lbs. 15 oz.	2-3rds	Staggering, loss of power in legs, violent convulsions	Death in 19 min.

TABLE III.—Showing the Minimum Fatal Dose of Picrotoxine in Guinea-Pigs.

No.	Weight of Guinea-Pig.	Dose of Picrotoxine in parts of a grain.	Effects.	Result.
19	1 lb. 2 oz.	1-55th	Lethargy, followed by restlessness, with twitchings of ears	Recovery
20	1 lb. 6 oz.	1-50th	Dulness, quickened respiration, twitchings of ears and mouth	"
21	1 lb. 4 oz.	1-40th	Dulness, hurried respiration, twitchings, three severe fits, with tonic and clonic spasms	"
22	1 lb. 5 oz.	1-35th	Lethargy, restlessness, twitchings of ears and mouth, loss of power in hind legs	"
23	1 lb. 5 oz.	1-30th	Drowsiness, hurried breathing, restlessness, three fits, then constant convulsions	Death in 123 m.
24	1 lb. 2 oz.	1-30th	Lethargy, twitchings, violent convulsions	Death in 62 min.
25	1 lb.	1-30th	Liveliness, startings, violent convulsions	Death in 40 min.
26	1 lb. 2 oz.	1-20th	Lethargy, twitchings, violent convulsions	Death in 75 min.
27	1 lb. 6 oz.	1-4th	Lethargy, hurried breathing, startings, violent convulsions	Death in 25 min.

These tables demonstrate that one-twentieth of a grain of picrotoxine may be regarded as the minimum fatal dose in a rabbit weighing about three pounds, and that one-thirtieth of a grain may be regarded as the minimum fatal dose for a guinea-pig weighing about a pound and a quarter. This point having been satisfactorily settled, the next experiment was directed to ascertain whether, as had been supposed, the action of the picrotoxine could be modified or controlled by chloral hydrate.

Experiment XXVIII.—A vigorous rabbit, weighing exactly three pounds, was procured, and to it one-twentieth of a grain of picrotoxine was administered by hypodermic injection, ten grains of chloral hydrate being simultaneously administered in the same way. Ten minutes after the injection, the rabbit was heavy and dull; and, five minutes later, its bowels having in the meantime acted very freely, there was super-added to the dulness some drowsiness. It still rested upon its feet, but its head drooped to one side. The breathing was exceedingly rapid. Twenty minutes after the injection, it was drowsy, but still sitting up, and able to move away at once when pinched or disturbed. The